Mesenchymal stromal cell-based treatment of jaw osteoradionecrosis in Swine.

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Public Summary:
Osteoradionecrosis (ORN) of the mandible is a common and serious complication of radiation therapy of head and neck cancers, with an incidence ranging from 4% to 30%. Treatment of ORN, especially advanced ORN, is a challenging clinical issue, and there is no well-established large animal model for basic and clinical studies. Recent studies have demonstrated that bone marrow mesenchymal stromal cells (BMMSCs), which are multipotent postnatal stem cells with the capacity to differentiate into osteoblasts, chondrocytes, adipocytes, and neural cells, have therapeutic potential in irradiated tissues. The most significant differentiating pathway of BMMSCs is development into osteogenic lineages and vascular tissues, which has been demonstrated in vitro and in vivo. When transplanted subcutaneously into immunocompromised mice, BMMSCs generate organ-like structures containing newly formed bone and associated hematopoietic marrow components. BMMSCs also have the potential to regulate immune and inflammatory responses. BMMSCs have been used to treat a variety if medical conditions in humans, including bone fracture, severe aplastic anemia, systemic lupus erythematosus, and acute graft-versus-host disease. In this study we used swine as a preclinical model to generate advanced ORN to show that the defect could be ameliorated by treatment with autologous BMMSC implantation. Due to the high similarity between swine and humans in tissue histology and organ functions, this experiments provided important clinical information that mesenchymal stem cell implantation may be a effective therapeutic approach for ORN.

Scientific Abstract:
Jaw osteoradionecrosis (ORN) is a common and serious complication of radiation therapy for head and neck cancers. Bone marrow mesenchymal stromal cells (BMMSCs) are multipotent postnatal stem cells and have been widely used in clinical therapies. In the present study, we generated the mandibular ORN model in swine using a combination of single-dose 25-Gy irradiation and tooth extraction. A typical ORN phenotype, including loss of bone regeneration capacity and collagen collapse with the obliteration of vessels, gradually appeared after irradiation. After autologous BMMSC transplantation, new bone and vessels were regenerated, and the advanced mandibular ORN was treated successfully. In summary, we developed a swine model of jaw ORN, and our results indicate that autologous BMMSC transplantation may be a promising therapeutic approach for ORN.